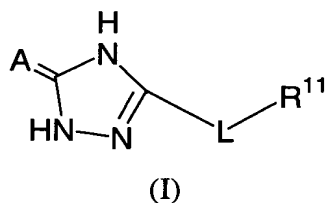


## WHAT IS CLAIMED IS:

## 1. A compound of formula (I):



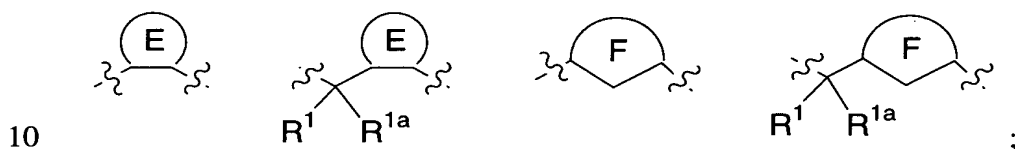
5

or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein;

A is O or S;

L is  $-(CR^2R^3)-(CR^4R^5)_n-(CR^6R^7)_{n1}-$ ;

alternatively, L is selected from the group:



$R^1$  is, independently at each occurrence, H,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl, or  $C_{2-6}$  alkynyl;

$R^{1a}$  is, independently at each occurrence, H,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl, or  $C_{2-6}$  alkynyl;

15  $R^2$  is  $Q^1$ ,  $C_{1-6}$  alkylene- $Q^1$ ,  $C_{2-6}$  alkenylene- $Q^1$ ,  $C_{2-6}$  alkynylene- $Q^1$ ,  
 $-(CR^aR^{a1})_rO(CR^aR^{a1})_s-Q^1$ ,  $-(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q^1$ ,  
 $-(CR^aR^{a1})_rC(O)(CR^aR^{a1})_s-Q^1$ ,  $-(CR^aR^{a1})_rC(O)O(CR^aR^{a1})_s-Q^1$ ,  
 $-(CR^aR^{a1})_rOC(O)(CR^aR^{a1})_s-Q^1$ ,  $-(CR^aR^{a1})_rC(O)NR^aR^{a1}$ ,  
 $-(CR^aR^{a1})_rC(O)NR^a(CR^aR^{a1})_s-Q^1$ ,  $-(CR^aR^{a1})_rNR^aC(O)(CR^aR^{a1})_s-Q^1$ ,  
 20  $-(CR^aR^{a1})_rOC(O)O(CR^aR^{a1})_s-Q^1$ ,  $-(CR^aR^{a1})_rOC(O)NR^a(CR^aR^{a1})_s-Q^1$ ,  
 $-(CR^aR^{a1})_rNR^aC(O)NR^a(CR^aR^{a1})_s-Q^1$ ,  $-(CR^aR^{a1})_rS(O)_p(CR^aR^{a1})_s-Q^1$ ,  
 $-(CR^aR^{a1})_rSO_2NR^a(CR^aR^{a1})_s-Q^1$ ,  $-(CR^aR^{a1})_rNR^aSO_2(CR^aR^{a1})_s-Q^1$ , or  
 $-(CR^aR^{a1})_rNR^aSO_2NR^a(CR^aR^{a1})_s-Q^1$ ;

$R^3$  is Q,  $C_{1-6}$  alkylene-Q,  $C_{2-6}$  alkenylene-Q,  $C_{2-6}$  alkynylene-Q,  
 25  $-(CR^aR^{a1})_rO(CR^aR^{a1})_s-Q$ ,  $-(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q$ ,  
 $-(CR^aR^{a1})_rC(O)(CR^aR^{a1})_s-Q$ ,  $-(CR^aR^{a1})_rC(O)O(CR^aR^{a1})_s-Q$

$-(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_r\text{C}(\text{O})\text{NR}^{\text{a}}\text{R}^{\text{a1}}, -(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_r\text{C}(\text{O})\text{NR}^{\text{a}}(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_s-\text{Q},$   
 $-(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_r\text{NR}^{\text{a}}\text{C}(\text{O})(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_s-\text{Q}, -(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_r\text{S}(\text{O})_p(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_s-\text{Q},$   
 $-(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_r\text{SO}_2\text{NR}^{\text{a}}(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_s-\text{Q},$  or  $-(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_r\text{NR}^{\text{a}}\text{SO}_2(\text{CR}^{\text{a}}\text{R}^{\text{a1}})_s-\text{Q};$

Q is, independently at each occurrence, H,  $\text{CHF}_2$ ,  $\text{CH}_2\text{F}$ ,  $\text{CF}_3$ , a  $\text{C}_{3-13}$   
 5 carbocycle substituted with 0-5  $\text{R}^{\text{d}}$ , or a 5-14 membered heterocycle consisting of  
 carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  
 $\text{S}(\text{O})_p$ , and substituted with 0-5  $\text{R}^{\text{d}}$ ;

10  $\text{Q}^1$  is, independently at each occurrence, H, a  $\text{C}_{3-13}$  carbocycle substituted  
 with 0-5  $\text{R}^{\text{d}}$ , or a 5-14 membered heterocycle consisting of carbon atoms and 1-4  
 heteroatoms selected from the group consisting of N,  $\text{NR}^{10}$ , O, and  $\text{S}(\text{O})_p$ , and  
 substituted with 0-5  $\text{R}^{\text{d}}$ ;

$\text{R}^4$  is H,  $\text{C}_{1-6}$  alkyl substituted with 0-1  $\text{R}^{\text{b}}$ ,  $\text{C}_{2-6}$  alkenyl substituted with 0-1  
 $\text{R}^{\text{b}}$ , or  $\text{C}_{2-6}$  alkynyl substituted with 0-1  $\text{R}^{\text{b}}$ ;

15  $\text{R}^5$  is H,  $\text{C}_{1-6}$  alkyl substituted with 0-1  $\text{R}^{\text{b}}$ ,  $\text{C}_{2-6}$  alkenyl substituted with 0-1  
 $\text{R}^{\text{b}}$ , or  $\text{C}_{2-6}$  alkynyl substituted with 0-1  $\text{R}^{\text{b}}$ ;

$\text{R}^6$  is H,  $\text{C}_{1-6}$  alkyl substituted with 0-1  $\text{R}^{\text{b}}$ ,  $\text{C}_{2-6}$  alkenyl substituted with 0-1  
 $\text{R}^{\text{b}}$ , or  $\text{C}_{2-6}$  alkynyl substituted with 0-1  $\text{R}^{\text{b}}$ ;

$\text{R}^7$  is H,  $\text{C}_{1-6}$  alkyl substituted with 0-1  $\text{R}^{\text{b}}$ ,  $\text{C}_{2-6}$  alkenyl substituted with 0-1  
 $\text{R}^{\text{b}}$ , or  $\text{C}_{2-6}$  alkynyl substituted with 0-1  $\text{R}^{\text{b}}$ ;

20 n is 0 or 1;

n1 is 0 or 1;

alternatively,  $\text{R}^2$  and  $\text{R}^3$ , together with the carbon atom to which they are  
 attached, combine to form a 3-8 membered carbocyclic or heterocyclic ring consisting  
 of carbon atoms and 0-2 ring heteroatoms selected from O, N,  $\text{NR}^{10}$ , and  $\text{S}(\text{O})_p$ , and  
 25 0-2 double bonds, and substituted with 0-3  $\text{R}^9$ ; and the carbocyclic or heterocyclic  
 ring is optionally fused to a 5-6 membered carbocycle or heterocycle consisting of  
 carbon atoms and 0-2 ring heteroatoms selected from O, N,  $\text{NR}^{10}$ , and  $\text{S}(\text{O})_p$ , and 0-2  
 double bonds, and substituted with 0-3  $\text{R}^9$ ;

30 alternatively, when n is 1,  $\text{R}^4$  and  $\text{R}^5$ , together with the carbon atom to which  
 they are attached, combine to form a 3-8 membered carbocyclic or heterocyclic ring

consisting of carbon atoms and 0-2 ring heteroatoms selected from O, N, NR<sup>10</sup>, and S(O)<sub>p</sub>, and 0-2 double bonds, and substituted with 0-3 R<sup>9</sup>; and the carbocyclic or heterocyclic ring is optionally fused to a 5-6 membered carbocycle or heterocycle consisting of carbon atoms and 0-2 ring heteroatoms selected from O, N, NR<sup>10</sup>, and S(O)<sub>p</sub>, and 0-2 double bonds, and substituted with 0-3 R<sup>9</sup>;

alternatively, when n1 is 1, R<sup>6</sup> and R<sup>7</sup>, together with the carbon atom to which they are attached, combine to form a 3-8 membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from O, N, NR<sup>10</sup>, and S(O)<sub>p</sub>, and 0-2 double bonds, and substituted with 0-3 R<sup>9</sup>; and the carbocyclic or heterocyclic ring is optionally fused to a 5-6 membered carbocycle or heterocycle consisting of carbon atoms and 0-2 ring heteroatoms selected from O, N, NR<sup>10</sup>, and S(O)<sub>p</sub>, and 0-2 double bonds, and substituted with 0-3 R<sup>9</sup>;

ring E is a 3-8 membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from O, N, NR<sup>10</sup>, and S(O)<sub>p</sub>, and 0-2 double bonds, and substituted with 0-3 R<sup>c</sup>; and the carbocyclic or heterocyclic ring is optionally fused to a 5-6 membered carbocycle or heterocycle consisting of carbon atoms and 0-2 ring heteroatoms selected from O, N, NR<sup>10</sup>, and S(O)<sub>p</sub>, and 0-2 double bonds, and substituted with 0-3 R<sup>9</sup>;

ring F is a 4-8 membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from O, N, NR<sup>10</sup>, and S(O)<sub>p</sub>, and 0-2 double bonds, and substituted with 0-3 R<sup>c</sup>; and the carbocyclic or heterocyclic ring is optionally fused to a 5-6 membered carbocycle or heterocycle consisting of carbon atoms and 0-2 ring heteroatoms selected from O, N, NR<sup>10</sup>, and S(O)<sub>p</sub>, and 0-2 double bonds, and substituted with 0-3 R<sup>9</sup>;

R<sup>11</sup> is -W-U-X-Y-Z-U<sup>a</sup>-X<sup>a</sup>-Y<sup>a</sup>-Z<sup>a</sup>;

W is (CR<sup>a</sup>R<sup>a1</sup>)<sub>m</sub>, C<sub>2-3</sub> alkenylene, or C<sub>2-3</sub> alkynylene;

U is O, C(O), CR<sup>a</sup>(OH), C(O)O, OC(O), C(O)NR<sup>a1</sup>, NR<sup>a1</sup>C(O), OC(O)O, OC(O)NR<sup>a1</sup>, NR<sup>a1</sup>C(O)O, NR<sup>a1</sup>C(O)NR<sup>a1</sup>, S(O)<sub>p</sub>, S(O)<sub>p</sub>NR<sup>a1</sup>, NR<sup>a1</sup>S(O)<sub>p</sub>, or NR<sup>a1</sup>SO<sub>2</sub>NR<sup>a1</sup>;

X is absent or is C<sub>1-3</sub> alkylene, C<sub>2-3</sub> alkenylene, or C<sub>2-3</sub> alkynylene;

Y is absent or is O, NR<sup>a1</sup>, S(O)<sub>p</sub>, or C(O);

Z is a C<sub>3-13</sub> carbocycle substituted with 0-5 R<sup>b</sup>, or a 5-14 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub> and substituted with 0-5 R<sup>b</sup>;

5 U<sup>a</sup> is absent or is O, NR<sup>a1</sup>, C(O), CR<sup>a</sup>(OH), C(O)O, OC(O), C(O)NR<sup>a1</sup>, NR<sup>a1</sup>C(O), OC(O)O, OC(O)NR<sup>a1</sup>, NR<sup>a1</sup>C(O)O, NR<sup>a1</sup>C(O)NR<sup>a1</sup>, S(O)<sub>p</sub>, S(O)<sub>p</sub>NR<sup>a1</sup>, NR<sup>a1</sup>S(O)<sub>p</sub>, or NR<sup>a1</sup>SO<sub>2</sub>NR<sup>a1</sup>;

X<sup>a</sup> is absent or is C<sub>1-10</sub> alkylene, C<sub>2-10</sub> alkenylene, or C<sub>2-10</sub> alkynylene;

Y<sup>a</sup> is absent or is O, NR<sup>a1</sup>, S(O)<sub>p</sub>, or C(O);

10 Z<sup>a</sup> is H, a C<sub>3-13</sub> carbocycle substituted with 0-5 R<sup>c</sup>, or a 5-14 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub> and substituted with 0-5 R<sup>c</sup>;

provided that U, Y, Z, U<sup>a</sup>, Y<sup>a</sup>, and Z<sup>a</sup> do not combine to form a N-N, N-O, O-N, O-O, S(O)<sub>p</sub>-O, O-S(O)<sub>p</sub> or S(O)<sub>p</sub>-S(O)<sub>p</sub> group;

15 R<sup>a</sup> is, independently at each occurrence, H, C<sub>1-6</sub> alkyl, phenyl, or benzyl;

R<sup>a1</sup> is, independently at each occurrence, H, C<sub>1-6</sub> alkyl substituted with 0-1 R<sup>c1</sup>, C<sub>2-6</sub> alkenyl substituted with 0-1 R<sup>c1</sup>, C<sub>2-6</sub> alkynyl substituted with 0-1 R<sup>c1</sup>, or -(CH<sub>2</sub>)<sub>r</sub>-3-8 membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from N, NR<sup>a2</sup>, O, and S(O)<sub>p</sub>, and substituted with  
20 0-3 R<sup>c1</sup>;

alternatively, R<sup>a</sup> and R<sup>a1</sup> when attached to a nitrogen, together with the nitrogen to which they are attached, combine to form a 5 or 6 membered heterocycle consisting of carbon atoms and from 0-1 additional heteroatoms selected from N, NR<sup>a2</sup>, O, and S(O)<sub>p</sub>;

25 R<sup>a2</sup> is, independently at each occurrence, C<sub>1-4</sub> alkyl, phenyl, or benzyl;

R<sup>a3</sup> is, independently at each occurrence, H, C<sub>1-6</sub> alkyl substituted with R<sup>c1</sup>, C<sub>2-6</sub> alkenyl substituted with 0-1 R<sup>c1</sup>, C<sub>2-6</sub> alkynyl substituted with 0-1 R<sup>c1</sup>, or -(CH<sub>2</sub>)<sub>r</sub>-3-8 membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from N, NR<sup>a2</sup>, O, and S(O)<sub>p</sub>, and substituted with  
30 0-3 R<sup>c1</sup>;

$R^b$ , at each occurrence, is independently selected from  $C_{1-6}$  alkyl substituted with 0-1  $R^{c1}$ ,  $OR^a$ ,  $SR^a$ , Cl, F, Br, I, =O, CN,  $NO_2$ ,  $-NR^aR^{a1}$ ,  $-C(O)R^a$ ,  $-C(O)OR^a$ ,  $-C(O)NR^aR^{a1}$ ,  $-C(S)NR^aR^{a1}$ ,  $-NR^aC(O)NR^aR^{a1}$ ,  $-OC(O)NR^aR^{a1}$ ,  $-NR^aC(O)OR^a$ ,  $-S(O)_2NR^aR^{a1}$ ,  $-NR^aS(O)_2R^{a3}$ ,  $-NR^aS(O)_2NR^aR^{a1}$ ,  $-OS(O)_2NR^aR^{a1}$ ,  
 5  $-S(O)_pR^{a3}$ ,  $-CF_3$ ,  $-CF_2CF_3$ ,  $-CHF_2$ ,  $-CH_2F$ , or phenyl;

$R^c$  is, independently at each occurrence, H,  $OR^a$ , Cl, F, Br, I, =O, CN,  $NO_2$ ,  $CF_3$ ,  $-CF_2CF_3$ ,  $CH_2F$ ,  $CHF_2$ ,  $-(CR^aR^{a1})_rNR^aR^{a1}$ ,  $-(CR^aR^{a1})_rC(=NCN)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rC(=NR^a)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rC(=NOR^a)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rC(O)NR^aOH$ ,  $-(CR^aR^{a1})_rC(O)R^{a1}$ ,  $-(CR^aR^{a1})_rC(O)OR^{a1}$ ,  $-(CR^aR^{a1})_rC(S)OR^{a1}$ ,  
 10  $-(CR^aR^{a1})_rC(O)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rNR^aC(O)R^{a1}$ ,  $-(CR^aR^{a1})_rC(S)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rOC(O)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rNR^aC(O)OR^{a1}$ ,  $-(CR^aR^{a1})_rNR^aC(O)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rS(O)_pR^{a3}$ ,  $-(CR^aR^{a1})_rSO_2NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rNR^aSO_2R^{a3}$ ,  $-(CR^aR^{a1})_rNR^aSO_2NR^aR^{a1}$ ,  $C_{1-6}$  alkyl substituted with 0-2  $R^{c1}$ ,  $C_{2-6}$  alkenyl substituted with 0-2  $R^{c1}$ ,  $C_{2-6}$  alkynyl substituted with 0-2  $R^{c1}$ ,  $-(CR^aR^{a1})_r-C_{3-10}$   
 15 carbocycle substituted with 0-2  $R^{c1}$ , or  $-(CR^aR^{a1})_r-5-14$  membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ , and substituted with 0-2  $R^{c1}$ ;

alternatively, when two  $R^c$  groups are attached to the same carbon atom, they form a 3-8 membered carbocyclic or heterocyclic spiro ring C substituted with 0-2  
 20  $R^{c1}$  and consisting of carbon atoms, 0-4 ring heteroatoms selected from O, N, and  $S(O)_p$ , and 0-2 double bonds, provided that ring C contains other than a S-S, O-O, or S-O bond;

alternatively, when two  $R^c$  groups are attached to adjacent carbon atoms, together with the carbon atoms to which they are attached they form a 5-7 membered  
 25 carbocyclic or heterocyclic ring D substituted with 0-2  $R^{c1}$  and consisting of carbon atoms, 0-2 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ , and 0-3 double bonds;

$R^{c1}$  is, independently at each occurrence, H,  $C_{1-4}$  alkyl,  $OR^a$ , Cl, F, Br, I, =O,  $CF_3$ , CN,  $NO_2$ ,  $-C(O)R^a$ ,  $-C(O)OR^a$ ,  $-C(O)NR^aR^a$ , or  $-S(O)_pR^a$ ;

$R^d$  is, independently at each occurrence,  $C_{1-6}$  alkyl,  $OR^a$ , Cl, F, Br, I, =O, CN,  $NO_2$ ,  $-NR^aR^{a1}$ ,  $-C(O)R^a$ ,  $-C(O)OR^a$ ,  $-C(O)NR^aR^{a1}$ ,  $-C(S)NR^aR^{a1}$ ,  $-NR^aC(O)NR^aR^{a1}$ ,  $-OC(O)NR^aR^{a1}$ ,  $-NR^aC(O)OR^a$ ,  $-S(O)_2NR^aR^{a1}$ ,  $-NR^aS(O)_2R^{a3}$ ,  $-NR^aS(O)_2NR^aR^{a1}$ ,  $-OS(O)_2NR^aR^{a1}$ ,  $-S(O)_pR^{a3}$ ,  $-CF_3$ ,  $-CF_2CF_3$ ,  $C_{3-10}$  carbocycle, or a 5-14 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ ;

$R^e$  is, independently at each occurrence, H,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy, phenoxy, benzoxy,  $C_{3-10}$  carbocycle substituted with 0-2  $R^{c1}$ , or a 5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ , and substituted with 0-2  $R^{c1}$ ;

$R^9$  is, independently at each occurrence, H,  $-(CR^aR^{a1})_rNR^aR^{a1}$ ,  $-(CR^aR^{a1})_rC(O)NR^aOH$ ,  $-(CR^aR^{a1})_rC(O)(CR^aR^{a1})_sR^e$ ,  $-(CR^aR^{a1})_rC(O)OR^{a1}$ ,  $-(CR^aR^{a1})_rC(S)OR^{a1}$ ,  $-(CR^aR^{a1})_rC(O)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rNR^aC(O)R^{a1}$ ,  $-(CR^aR^{a1})_rC(S)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rOC(O)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rNR^aC(O)OR^{a1}$ ,  $-(CR^aR^{a1})_rNR^aC(O)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rS(O)_pR^{a3}$ ,  $-(CR^aR^{a1})_rSO_2NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rNR^aSO_2R^{a3}$ ,  $-(CR^aR^{a1})_rNR^aSO_2NR^aR^{a1}$ ,  $C_{1-6}$  alkyl substituted with 0-2  $R^{c1}$ ,  $C_{2-6}$  alkenyl substituted with 0-2  $R^{c1}$ ,  $C_{2-6}$  alkynyl substituted with 0-2  $R^{c1}$ ,  $-(CR^aR^{a1})_rC_{3-10}$  carbocycle substituted with 0-2  $R^{c1}$ , or  $-(CR^aR^{a1})_r$ -5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ , and substituted with 0-2  $R^{c1}$ ;

$R^{10}$  is, independently at each occurrence, H,  $-(CR^aR^{a1})_tNR^aR^{a1}$ ,  $-(CR^aR^{a1})_rC(O)NR^aOH$ ,  $-(CR^aR^{a1})_rC(O)(CR^aR^{a1})_sR^e$ ,  $-(CR^aR^{a1})_rC(O)OR^{a1}$ ,  $-(CR^aR^{a1})_rC(S)OR^{a1}$ ,  $-(CR^aR^{a1})_rC(O)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_tNR^aC(O)R^{a1}$ ,  $-(CR^aR^{a1})_rC(S)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_tOC(O)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_tNR^aC(O)OR^{a1}$ ,  $-(CR^aR^{a1})_tNR^aC(O)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rS(O)_pR^{a3}$ ,  $-(CR^aR^{a1})_rSO_2NR^aR^{a1}$ ,  $-(CR^aR^{a1})_tNR^aSO_2R^{a3}$ ,  $-(CR^aR^{a1})_tNR^aSO_2NR^aR^{a1}$ ,  $C_{1-6}$  alkyl substituted with 0-2  $R^{c1}$ ,  $C_{2-6}$  alkenyl substituted with 0-2  $R^{c1}$ ,  $C_{2-6}$  alkynyl substituted with 0-2  $R^{c1}$ ,

$-(\text{CR}^a\text{R}^a\text{R}^a)_r\text{-C}_{3-10}$  carbocycle substituted with 0-2  $\text{R}^c$ , or  $-(\text{CR}^a\text{R}^a\text{R}^a)_r\text{-5-10}$  membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, and substituted with 0-2  $\text{R}^c$ ;

m, at each occurrence, is selected from 0, 1, 2 and 3;

5 p, at each occurrence, is selected from 0, 1, and 2;

r, at each occurrence, is selected from 0, 1, 2, 3, and 4;

s, at each occurrence, is selected from 0, 1, 2, 3, and 4; and

t, at each occurrence, is selected from 1, 2, 3, and 4;

provided that:

10 (i) when L is  $\text{CR}^2\text{R}^3$  or  $\text{CR}^2\text{R}^3\text{CH}_2$ ,  $\text{Z}^a$  is other than H;

(ii) when Z is cyclohexyl, benzodiazepinyl or a nitrogen-containing 10-membered bicyclic heteroaryl, then  $\text{Z}^a$  is other than phenyl or phenyl fused carbocycle;

(iii) when Z is phenyl, and  $\text{Z}^a$  is oxazolyl, then  $\text{R}^c$  is other than phenyl;

15 (iv) when Z is a  $\text{C}_{5-7}$  cycloalkyl, then  $\text{R}^b$  is other than phenyl;

(v) when A is S, and L is 1,2-phenylene, then  $\text{Z}^a$  is other than thienyl or phenyl substituted with triazolthione;

(vi) when A is S, L is  $\text{CH}_2$ , U-X-Y forms O or S, and Z is a benzopyranlyl, quinazolinyl, or triazinyl ring, then  $\text{Z}^a$  is other than phenyl;

20 (vii) when A is S, L is 4,5,6-7-tetrahydrobenzothienyl, and U-X-Y forms  $\text{C}(\text{O})\text{NH}$ , Z is other than 5,6,7,8-tetrahydro-benzothieno[2,3-b]pyridinyl; and

(viii) when L is 1,2-phenylene or 1,3-phenylene, then  $\text{U}^a\text{-X}^a\text{-Y}^a$  forms other than  $\text{C}_{1-2}$  alkylene or  $\text{CH}_2\text{NR}^a$ .

25 2. A compound according to Claim 1, wherein:

$\text{R}^2$  is  $\text{Q}^1$ ,  $\text{C}_{1-6}$  alkylene- $\text{Q}^1$ ,  $\text{C}_{2-6}$  alkenylene- $\text{Q}^1$ ,  $\text{C}_{2-6}$  alkynylene- $\text{Q}^1$ ,  
 $-(\text{CR}^a\text{R}^a\text{R}^a)_r\text{O}(\text{CR}^a\text{R}^a\text{R}^a)_s\text{-Q}^1$ ,  $-(\text{CR}^a\text{R}^a\text{R}^a)_r\text{NR}^a(\text{CR}^a\text{R}^a\text{R}^a)_s\text{-Q}^1$ ,  
 $-(\text{CR}^a\text{R}^a\text{R}^a)_r\text{C}(\text{O})(\text{CR}^a\text{R}^a\text{R}^a)_s\text{-Q}^1$ ,  $-(\text{CR}^a\text{R}^a\text{R}^a)_r\text{C}(\text{O})\text{O}(\text{CR}^a\text{R}^a\text{R}^a)_s\text{-Q}^1$ ,  
 $-(\text{CR}^a\text{R}^a\text{R}^a)_r\text{OC}(\text{O})(\text{CR}^a\text{R}^a\text{R}^a)_s\text{-Q}^1$ ,  $-(\text{CR}^a\text{R}^a\text{R}^a)_r\text{C}(\text{O})\text{NR}^a\text{R}^a$ ,  
 30  $-(\text{CR}^a\text{R}^a\text{R}^a)_r\text{C}(\text{O})\text{NR}^a(\text{CR}^a\text{R}^a\text{R}^a)_s\text{-Q}^1$ ,  $-(\text{CR}^a\text{R}^a\text{R}^a)_r\text{NR}^a\text{C}(\text{O})(\text{CR}^a\text{R}^a\text{R}^a)_s\text{-Q}^1$ ,  
 $-(\text{CR}^a\text{R}^a\text{R}^a)_r\text{S}(\text{O})_p(\text{CR}^a\text{R}^a\text{R}^a)_s\text{-Q}^1$ ,  $-(\text{CR}^a\text{R}^a\text{R}^a)_r\text{SO}_2\text{NR}^a(\text{CR}^a\text{R}^a\text{R}^a)_s\text{-Q}^1$ , or

$-(\text{CR}^a\text{R}^{a1})_r\text{NR}^a\text{SO}_2(\text{CR}^a\text{R}^{a1})_s\text{-Q}^1$ ;

- $\text{R}^3$  is Q,  $\text{C}_{1-6}$  alkylene-Q,  $\text{C}_{2-6}$  alkenylene-Q,  $\text{C}_{2-6}$  alkynylene-Q,  
 $-(\text{CH}_2)_r\text{O}(\text{CH}_2)_s\text{-Q}$ ,  $-(\text{CH}_2)_r\text{NR}^a(\text{CH}_2)_s\text{-Q}$ ,  $-(\text{CH}_2)_r\text{C}(\text{O})(\text{CH}_2)_s\text{-Q}$ ,  
 $-(\text{CH}_2)_r\text{C}(\text{O})\text{O}(\text{CH}_2)_s\text{-Q}$ ,  $-(\text{CH}_2)_r\text{C}(\text{O})\text{NR}^a\text{R}^{a1}$ ,  $-(\text{CH}_2)_r\text{C}(\text{O})\text{NR}^a(\text{CH}_2)_s\text{-Q}$ ,  
 5  $-(\text{CH}_2)_r\text{NR}^a\text{C}(\text{O})(\text{CH}_2)_s\text{-Q}$ ,  $-(\text{CH}_2)_r\text{S}(\text{O})_p(\text{CH}_2)_s\text{-Q}$ ,  $-(\text{CH}_2)_r\text{SO}_2\text{NR}^a(\text{CH}_2)_s\text{-Q}$ , or  
 $-(\text{CH}_2)_r\text{NR}^a\text{SO}_2(\text{CH}_2)_s\text{-Q}$ ;

$\text{R}^4$  is H,  $\text{C}_{1-6}$  alkyl substituted with 0-1  $\text{R}^b$ ,  $\text{C}_{2-6}$  alkenyl substituted with 0-1  $\text{R}^b$ , or  $\text{C}_{2-6}$  alkynyl substituted with 0-1  $\text{R}^b$ ;

- $\text{R}^5$  is H,  $\text{C}_{1-6}$  alkyl substituted with 0-1  $\text{R}^b$ ,  $\text{C}_{2-6}$  alkenyl substituted with 0-1  
 10  $\text{R}^b$ , or  $\text{C}_{2-6}$  alkynyl substituted with 0-1  $\text{R}^b$ ;

$\text{R}^6$  is H,  $\text{C}_{1-6}$  alkyl substituted with 0-1  $\text{R}^b$ ,  $\text{C}_{2-6}$  alkenyl substituted with 0-1  $\text{R}^b$ , or  $\text{C}_{2-6}$  alkynyl substituted with 0-1  $\text{R}^b$ ;

$\text{R}^7$  is H,  $\text{C}_{1-6}$  alkyl substituted with 0-1  $\text{R}^b$ ,  $\text{C}_{2-6}$  alkenyl substituted with 0-1  $\text{R}^b$ , or  $\text{C}_{2-6}$  alkynyl substituted with 0-1  $\text{R}^b$ ;

- 15 alternatively,  $\text{R}^2$  and  $\text{R}^3$ , together with the carbon atom to which they are attached, combine to form a 3-8 membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from O, N,  $\text{NR}^{10}$ , and  $\text{S}(\text{O})_p$ , and 0-2 double bonds, and substituted with 0-2  $\text{R}^9$ ;

- alternatively, when n is 1,  $\text{R}^4$  and  $\text{R}^5$  together with the carbon atom to which  
 20 they are attached combine to form a 3-8 membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from O, N,  $\text{NR}^{10}$ , and  $\text{S}(\text{O})_p$ , and 0-2 double bonds, and substituted with 0-2  $\text{R}^9$ ;

- alternatively, when n1 is 1,  $\text{R}^6$  and  $\text{R}^7$  together with the carbon atom to which  
 they are attached combine to form a 3-8 membered carbocyclic or heterocyclic ring  
 25 consisting of carbon atoms and 0-2 ring heteroatoms selected from O, N,  $\text{NR}^{10}$ , and  $\text{S}(\text{O})_p$ , and 0-2 double bonds, and substituted with 0-2  $\text{R}^9$ ;

ring E is a 3-8 membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from O, N,  $\text{NR}^{10}$ , and  $\text{S}(\text{O})_p$ , and 0-2 double bonds, and substituted with 0-3  $\text{R}^c$ ;



ring F is a 4-8 membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from O, N, NR<sup>10</sup>, and S(O)<sub>p</sub>, and 0-2 double bonds, and substituted with 0-3 R<sup>c</sup>;

W is (CR<sup>a</sup>R<sup>a1</sup>)<sub>m</sub>;

5 U is O, C(O), CR<sup>a</sup>(OH), C(O)O, OC(O), C(O)NR<sup>a1</sup>, NR<sup>a1</sup>C(O), S(O)<sub>p</sub>, S(O)<sub>p</sub>NR<sup>a1</sup>, or NR<sup>a1</sup>S(O)<sub>p</sub>;

X is absent or is C<sub>1-3</sub> alkylene;

Z is a C<sub>3-8</sub> cycloalkyl substituted with 0-5 R<sup>b</sup>, a C<sub>3-8</sub> cycloalkenyl substituted with 0-5 R<sup>b</sup>, phenyl substituted with 0-5 R<sup>b</sup>, naphthyl substituted with 0-5 R<sup>b</sup>, or a  
10 5-14 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub> and substituted with 0-5 R<sup>b</sup>;

U<sup>a</sup> is absent or is O, NR<sup>a1</sup>, C(O), CR<sup>a</sup>(OH), C(O)O, C(O)NR<sup>a1</sup>, NR<sup>a1</sup>C(O), S(O)<sub>p</sub>, S(O)<sub>p</sub>NR<sup>a1</sup>, or NR<sup>a1</sup>S(O)<sub>p</sub>;

X<sup>a</sup> is absent or is C<sub>1-4</sub> alkylene, C<sub>2-4</sub> alkenylene, or C<sub>2-4</sub> alkynylene;

15 Y<sup>a</sup> is absent or is O or NR<sup>a1</sup>;

Z<sup>a</sup> is a C<sub>6-13</sub> carbocycle substituted with 0-5 R<sup>c</sup>, or a 5-14 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, and substituted with 0-5 R<sup>c</sup>;

R<sup>a</sup> is, independently at each occurrence, H, C<sub>1-6</sub> alkyl, phenyl, or benzyl;

20 R<sup>a1</sup> is, independently at each occurrence, H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, and -(CH<sub>2</sub>)<sub>r</sub>-3-8 membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from N, NR<sup>a2</sup>, O, and S(O)<sub>p</sub>;

alternatively, R<sup>a</sup> and R<sup>a1</sup> when attached to a nitrogen, together with the nitrogen to which they are attached, combine to form a 5 or 6 membered heterocycle  
25 consisting of carbon atoms and from 0-1 additional heteroatoms selected from N, NR<sup>a2</sup>, O, and S(O)<sub>p</sub>;

R<sup>c</sup> is, independently at each occurrence, H, OR<sup>a</sup>, Cl, F, Br, =O, CN, NO<sub>2</sub>, CF<sub>3</sub>, CH<sub>2</sub>F, CHF<sub>2</sub>, -CF<sub>2</sub>CF<sub>3</sub>, -(CR<sup>a</sup>R<sup>a1</sup>)<sub>r</sub>NR<sup>a</sup>R<sup>a1</sup>, -(CR<sup>a</sup>R<sup>a1</sup>)<sub>r</sub>C(O)R<sup>a1</sup>, -(CR<sup>a</sup>R<sup>a1</sup>)<sub>r</sub>C(O)OR<sup>a1</sup>, -(CR<sup>a</sup>R<sup>a1</sup>)<sub>r</sub>C(O)NR<sup>a</sup>R<sup>a1</sup>, -(CR<sup>a</sup>R<sup>a1</sup>)<sub>r</sub>NR<sup>a</sup>C(O)R<sup>a1</sup>,

$-(\text{CR}^a\text{R}^{a1})_r\text{S}(\text{O})_p\text{Ra}^3$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{SO}_2\text{NR}^a\text{Ra}^1$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{NR}^a\text{SO}_2\text{Ra}^3$ ,  $\text{C}_{1-6}$  alkyl substituted with 0-1  $\text{R}^{\text{c}1}$ ,  $\text{C}_{2-6}$  alkenyl substituted with 0-1  $\text{R}^{\text{c}1}$ ,  $\text{C}_{2-6}$  alkynyl substituted with 0-1  $\text{R}^{\text{c}1}$ ,  $-(\text{CH}_2)_r\text{-C}_{3-6}$  carbocycle substituted with 0-2  $\text{R}^{\text{c}1}$ , or  $-(\text{CH}_2)_r\text{-5-6}$  membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $\text{S}(\text{O})_p$ , and substituted with 0-2  $\text{R}^{\text{c}1}$ ; alternatively, when two  $\text{R}^{\text{c}}$  groups are attached to the same carbon atom, they form a 3-8 membered carbocyclic or heterocyclic spiro ring C substituted with 0-2  $\text{R}^{\text{c}1}$  and consisting of carbon atoms, 0-4 ring heteroatoms selected from O, N, and  $\text{S}(\text{O})_p$ , and 0-2 double bonds, provided that ring C contains other than a S-S, O-O, or S-O bond;

alternatively, when two  $\text{R}^{\text{c}}$  groups are attached to adjacent carbon atoms, together with the carbon atoms to which they are attached they form a 5-7 membered carbocyclic or heterocyclic ring D substituted with 0-2  $\text{R}^{\text{c}1}$  and consisting of carbon atoms, 0-2 heteroatoms selected from the group consisting of N, O, and  $\text{S}(\text{O})_p$ , and 0-3 double bonds;

$\text{R}^{\text{d}}$  is, independently at each occurrence,  $\text{C}_{1-6}$  alkyl,  $\text{OR}^a$ , Cl, F, Br, =O, CN,  $\text{NO}_2$ ,  $-\text{NR}^a\text{Ra}^1$ ,  $-\text{C}(\text{O})\text{Ra}^a$ ,  $-\text{C}(\text{O})\text{OR}^a$ ,  $-\text{C}(\text{O})\text{NR}^a\text{Ra}^1$ ,  $-\text{S}(\text{O})_2\text{NR}^a\text{Ra}^1$ ,  $-\text{NR}^a\text{S}(\text{O})_2\text{Ra}^3$ ,  $-\text{S}(\text{O})_p\text{Ra}^3$ ,  $\text{CF}_3$ ,  $\text{C}_{3-6}$  carbocycle and a 5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $\text{S}(\text{O})_p$ ;

$\text{R}^9$  is, independently at each occurrence, H,  $-(\text{CR}^a\text{R}^{a1})_r\text{NR}^a\text{Ra}^1$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{C}(\text{O})\text{NR}^a\text{OH}$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{C}(\text{O})(\text{CR}^a\text{R}^{a1})_s\text{R}^e$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{C}(\text{O})\text{OR}^a$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{C}(\text{O})\text{NR}^a\text{Ra}^1$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{NR}^a\text{C}(\text{O})\text{Ra}^1$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{OC}(\text{O})\text{NR}^a\text{Ra}^1$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{NR}^a\text{C}(\text{O})\text{OR}^a$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{S}(\text{O})_p\text{Ra}^3$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{SO}_2\text{NR}^a\text{Ra}^1$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{NR}^a\text{SO}_2\text{Ra}^3$ ,  $\text{C}_{1-6}$  alkyl substituted with 0-2  $\text{R}^{\text{c}1}$ ,  $\text{C}_{2-6}$  alkenyl substituted with 0-2  $\text{R}^{\text{c}1}$ ,  $\text{C}_{2-6}$  alkynyl substituted with 0-2  $\text{R}^{\text{c}1}$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{-C}_{3-10}$  carbocycle substituted with 0-2  $\text{R}^{\text{c}1}$ , or  $-(\text{CR}^a\text{R}^{a1})_r\text{-5-10}$  membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $\text{S}(\text{O})_p$  and substituted with 0-2  $\text{R}^{\text{c}1}$ ; and

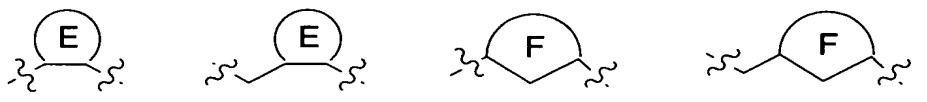
$\text{R}^{10}$  is, independently at each occurrence, H,  $-(\text{CR}^a\text{R}^{a1})_l\text{NR}^a\text{Ra}^1$ ,

$-(\text{CR}^a\text{R}^{a1})_r\text{C}(\text{O})\text{NR}^a\text{OH}$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{C}(\text{O})(\text{CR}^a\text{R}^{a1})_s\text{Re}$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{C}(\text{O})\text{OR}^{a1}$ ,  
 $-(\text{CR}^a\text{R}^{a1})_r\text{C}(\text{O})\text{NR}^a\text{R}^{a1}$ ,  $-(\text{CR}^a\text{R}^{a1})_t\text{NR}^a\text{C}(\text{O})\text{R}^{a1}$ ,  $-(\text{CR}^a\text{R}^{a1})_t\text{OC}(\text{O})\text{NR}^a\text{R}^{a1}$ ,  
 $-(\text{CR}^a\text{R}^{a1})_t\text{NR}^a\text{C}(\text{O})\text{OR}^{a1}$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{S}(\text{O})_p\text{R}^{a3}$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{SO}_2\text{NR}^a\text{R}^{a1}$ ,  
 $-(\text{CR}^a\text{R}^{a1})_t\text{NR}^a\text{SO}_2\text{R}^{a3}$ ,  $\text{C}_{1-6}$  alkyl substituted with 0-2  $\text{R}^{\text{c}1}$ ,  $\text{C}_{2-6}$  alkenyl substituted  
5 with 0-2  $\text{R}^{\text{c}1}$ ,  $\text{C}_{2-6}$  alkynyl substituted with 0-2  $\text{R}^{\text{c}1}$ ,  $-(\text{CR}^a\text{R}^{a1})_r\text{-C}_{3-10}$  carbocycle  
substituted with 0-2  $\text{R}^{\text{c}1}$ , or  $-(\text{CR}^a\text{R}^{a1})_r\text{-5-10}$  membered heterocycle consisting of  
carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  
 $\text{S}(\text{O})_p$  and substituted with 0-2  $\text{R}^{\text{c}1}$ .

10 3. A compound according to Claim 2, wherein:

L is  $-(\text{CR}^2\text{R}^3)-$ ,  $-(\text{CR}^2\text{R}^3)\text{-CH}_2-$ ,  $-(\text{CR}^2\text{R}^3)\text{-(CH}_2)_2-$ ,  $-\text{CH}_2\text{-(CR}^4\text{R}^5)-$ , or  $-\text{CH}_2\text{-(CR}^4\text{R}^5)\text{-CH}_2-$ ;

alternatively, L is selected from the group:



15  $\text{R}^2$  is  $\text{Q}^1$ ,  $\text{C}_{1-6}$  alkylene- $\text{Q}^1$ ,  $\text{C}_{2-6}$  alkenylene- $\text{Q}^1$ ,  $\text{C}_{2-6}$  alkynylene- $\text{Q}^1$ ,  
 $-(\text{CH}_2)_r\text{O}(\text{CH}_2)_s\text{-Q}^1$ ,  $-(\text{CH}_2)_r\text{NR}^a(\text{CH}_2)_s\text{-Q}^1$ ,  $-(\text{CH}_2)_r\text{C}(\text{O})(\text{CH}_2)_s\text{-Q}^1$ ,  
 $-(\text{CH}_2)_r\text{C}(\text{O})\text{O}(\text{CH}_2)_s\text{-Q}^1$ ,  $-(\text{CH}_2)_r\text{C}(\text{O})\text{NR}^a(\text{CH}_2)_s\text{-Q}^1$ ,  $-(\text{CH}_2)_r\text{NR}^a\text{C}(\text{O})(\text{CH}_2)_s\text{-Q}^1$ ,  
 $-(\text{CH}_2)_r\text{S}(\text{O})_p(\text{CH}_2)_s\text{-Q}^1$ ,  $-(\text{CH}_2)_r\text{SO}_2\text{NR}^a(\text{CH}_2)_s\text{-Q}^1$ , or  $-(\text{CH}_2)_r\text{NR}^a\text{SO}_2(\text{CH}_2)_s\text{-Q}^1$ ;

20  $\text{R}^3$  is Q,  $\text{C}_{1-6}$  alkylene-Q,  $\text{C}_{2-6}$  alkenylene-Q,  $\text{C}_{2-6}$  alkynylene-Q,  
 $-(\text{CH}_2)_r\text{O}(\text{CH}_2)_s\text{-Q}$ ,  $-(\text{CH}_2)_r\text{NR}^a(\text{CH}_2)_s\text{-Q}$ ,  $-(\text{CH}_2)_r\text{C}(\text{O})(\text{CH}_2)_s\text{-Q}$ ,  
 $-(\text{CH}_2)_r\text{C}(\text{O})\text{O}(\text{CH}_2)_s\text{-Q}$ ,  $-(\text{CH}_2)_r\text{C}(\text{O})\text{NR}^a\text{R}^{a1}$ ,  $-(\text{CH}_2)_r\text{C}(\text{O})\text{NR}^a(\text{CH}_2)_s\text{-Q}$ ,  
 $-(\text{CH}_2)_r\text{NR}^a\text{C}(\text{O})(\text{CH}_2)_s\text{-Q}$ ,  $-(\text{CH}_2)_r\text{S}(\text{O})_p(\text{CH}_2)_s\text{-Q}$ ,  $-(\text{CH}_2)_r\text{SO}_2\text{NR}^a(\text{CH}_2)_s\text{-Q}$ , or  
 $-(\text{CH}_2)_r\text{NR}^a\text{SO}_2(\text{CH}_2)_s\text{-Q}$ ;

25 Q is, independently at each occurrence, H, a  $\text{C}_{3-10}$  carbocycle substituted with  
 0-3  $\text{R}^{\text{d}}$ , or a 5-10 membered heterocycle consisting of carbon atoms and 1-4  
 heteroatoms selected from the group consisting of N, O, and  $\text{S}(\text{O})_p$ , and substituted  
 with 0-3  $\text{R}^{\text{d}}$ ;

$\text{R}^4$  is H or  $\text{C}_{1-6}$  alkyl;

$R^5$  is H or  $C_{1-6}$  alkyl;

alternatively,  $R^2$  and  $R^3$ , together with the carbon atom to which they are attached, combine to form a 3-8 membered carbocyclic or heterocyclic ring consisting of carbon atoms, 0-2 ring heteroatoms selected from O, N,  $NR^{10}$ , and  $S(O)_p$ , and 0-2

5 double bonds, and substituted with 0-2  $R^9$ ;

alternatively,  $R^4$  and  $R^5$ , together with the carbon atom to which they are attached, combine to form a 3-8 membered carbocyclic or heterocyclic ring consisting of carbon atoms, 0-2 ring heteroatoms selected from O, N,  $NR^{10}$ , and  $S(O)_p$ , and 0-2 double bonds, and substituted with 0-2  $R^9$ ;

10 ring E is a  $C_{3-7}$  cycloalkyl substituted with 0-2  $R^c$ , a  $C_{4-7}$  cycloalkenyl substituted with 0-2  $R^c$ , phenyl substituted with 0-3  $R^c$ , or a 5-7 membered heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from O, N,  $NR^{10}$ , and  $S(O)_p$ , and 0-2 double bonds, and substituted with 0-3  $R^c$ ;

ring F is a  $C_{4-7}$  cycloalkyl substituted with 0-2  $R^c$ , a  $C_{4-7}$  cycloalkenyl  
15 substituted with 0-2  $R^c$ , phenyl substituted with 0-3  $R^c$ , or a 5-7 membered heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from O, N,  $NR^{10}$ , and  $S(O)_p$ , and 0-2 double bonds, and substituted with 0-3  $R^c$ ;

U is O, C(O), C(O) $NR^{a1}$ ,  $NR^{a1}C(O)$ ,  $S(O)_p$ ,  $S(O)_pNR^{a1}$ , or  $NR^{a1}S(O)_p$ ;

X is absent, or is methylene or ethylene;

20 Z is a  $C_{4-8}$  cycloalkyl substituted with 0-3  $R^b$ , a  $C_{4-8}$  cycloalkenyl substituted with 0-3  $R^b$ , phenyl substituted with 0-4  $R^b$ , naphthyl substituted with 0-5  $R^b$ , or a heterocycle substituted with 0-3  $R^b$  and selected from the group: furanyl, tetrahydrofuranyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, isoxazolyl, 4,5-dihydro-isoxazolyl, thienyl, triazolyl, thiadiazolyl, oxadiazolyl, pyridyl,  
25 pyrimidinyl, piperazinyl, piperidinyl, pyranyl, pyrazinyl, pyrazolyl, pyridoimidazolyl, pyrrolidinyl, pyrrolyl, indolyl, indolynyl, benzimidazolyl, benzothiazinyl, benzofuranyl, benzothiophenyl, benzoxazolyl, benzthiazolyl, benztriazolyl, benzisoxazolyl, benzisothiazolyl, quinolynyl, tetrahydroquinolynyl, isoquinolynyl, tetrahydro-isoquinolynyl, indazolyl, isobenzofuranyl, isoindazolyl, isoindolynyl,  
30 isoindolyl, methylenedioxyphenyl, and quinazolinyl;

$U^a$  is absent or is O,  $NR^{a1}$ ,  $C(O)$ ,  $C(O)NR^{a1}$ ,  $NR^{a1}C(O)$ ,  $S(O)_p$ ,  $S(O)_pNR^{a1}$ , or  $NR^{a1}S(O)_p$ ;

$R^{a3}$  is, independently at each occurrence, H,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl, or  $-(CH_2)_r$ -3-8 membered carbocyclic or heterocyclic ring consisting of carbon atoms and 0-2 ring heteroatoms selected from N,  $NR^{a2}$ , O, and  $S(O)_p$ , and substituted with 0-3  $R^{c1}$ ;

$R^c$  is, independently at each occurrence, H,  $OR^a$ , Cl, F, Br, =O,  $CF_3$ ,  $CH_2F$ ,  $CHF_2$ ,  $-(CR^{a1}R^{a1})_rNR^{a1}$ ,  $-(CR^{a1}R^{a1})_rC(O)R^{a1}$ ,  $-(CR^{a1}R^{a1})_rC(O)OR^{a1}$ ,  $-(CR^{a1}R^{a1})_rC(O)NR^{a1}$ ,  $-(CR^{a1}R^{a1})_rNR^{a1}C(O)R^{a1}$ ,  $-(CR^{a1}R^{a1})_rS(O)_pR^{a3}$ ,  $-(CR^{a1}R^{a1})_rSO_2NR^{a1}$ ,  $-(CR^{a1}R^{a1})_rNR^{a1}SO_2R^{a3}$ ,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{3-6}$  cycloalkyl substituted with 0-2  $R^{c1}$ , phenyl substituted with 0-2  $R^{c1}$ , or a 5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ , and substituted with 0-2  $R^{c1}$ ;

alternatively, when two  $R^c$  groups are attached to the same carbon atom, they form a 5-7 membered carbocyclic or heterocyclic spiro ring C substituted with 0-2  $R^{c1}$  and consisting of carbon atoms, 0-4 ring heteroatoms selected from O, N, and  $S(O)_p$ , and 0-2 double bonds, provided that ring C contains other than a S-S, O-O, or S-O bond;

alternatively, when two  $R^c$  groups are attached to adjacent carbon atoms, together with the carbon atoms to which they are attached they form a 5-7 membered carbocyclic or heterocyclic ring D substituted with 0-2  $R^{c1}$  and consisting of carbon atoms, 0-2 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ , and 0-3 double bonds;

$R^d$  is, independently at each occurrence,  $C_{1-6}$  alkyl,  $OR^a$ , Cl, F, Br, =O,  $NR^{a1}$ ,  $-(CR^{a1}R^{a1})_rNR^{a1}$ ,  $-(CR^{a1}R^{a1})_rC(O)R^{a1}$ ,  $-(CR^{a1}R^{a1})_rC(O)OR^{a1}$ ,  $-(CR^{a1}R^{a1})_rC(O)NR^{a1}$ ,  $-(CR^{a1}R^{a1})_rNR^{a1}C(O)R^{a1}$ ,  $-(CR^{a1}R^{a1})_rS(O)_pR^{a3}$ ,  $-(CR^{a1}R^{a1})_rSO_2NR^{a1}$ ,  $CF_3$  or phenyl;

$R^9$  is, independently at each occurrence, H,  $-(CR^{a1}R^{a1})_rNR^{a1}$ ,  $-(CR^{a1}R^{a1})_rC(O)(CR^{a1}R^{a1})_sR^e$ ,  $-(CR^{a1}R^{a1})_rC(O)OR^{a1}$ ,  $-(CR^{a1}R^{a1})_rC(O)NR^{a1}$ ,  $-(CR^{a1}R^{a1})_rNR^{a1}C(O)R^{a1}$ ,  $-(CR^{a1}R^{a1})_rS(O)_pR^{a3}$ ,  $-(CR^{a1}R^{a1})_rSO_2NR^{a1}$ ,

5  $-(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_r\text{NR}^{\text{a}}\text{SO}_2\text{R}^{\text{a}3}$ ,  $\text{C}_{1-6}$  alkyl substituted with 0-2  $\text{R}^{\text{c}1}$ ,  $\text{C}_{2-6}$  alkenyl substituted with 0-2  $\text{R}^{\text{c}1}$ ,  $\text{C}_{2-6}$  alkynyl substituted with 0-2  $\text{R}^{\text{c}1}$ ,  $-(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_r\text{-C}_{3-10}$  carbocycle substituted with 0-2  $\text{R}^{\text{c}1}$ , or  $-(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_r\text{-5-10}$  membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $\text{S}(\text{O})_p$ , and substituted with 0-2  $\text{R}^{\text{c}1}$ ;

$\text{R}^{10}$  is, independently at each occurrence, H,  $-(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_t\text{NR}^{\text{a}}\text{R}^{\text{a}1}$ ,  $-(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_r\text{C}(\text{O})(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_s\text{R}^{\text{e}}$ ,  $-(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_r\text{C}(\text{O})\text{OR}^{\text{a}1}$ ,  $-(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_r\text{C}(\text{O})\text{NR}^{\text{a}}\text{R}^{\text{a}1}$ ,  $-(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_t\text{NR}^{\text{a}}\text{C}(\text{O})\text{R}^{\text{a}1}$ ,  $-(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_r\text{S}(\text{O})_p\text{R}^{\text{a}3}$ ,  $-(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_r\text{SO}_2\text{NR}^{\text{a}}\text{R}^{\text{a}1}$ ,  $-(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_t\text{NR}^{\text{a}}\text{SO}_2\text{R}^{\text{a}3}$ ,  $\text{C}_{1-6}$  alkyl substituted with 0-2  $\text{R}^{\text{c}1}$ ,  $\text{C}_{2-6}$  alkenyl substituted with 0-2  $\text{R}^{\text{c}1}$ ,  $\text{C}_{2-6}$  alkynyl substituted with 0-2  $\text{R}^{\text{c}1}$ ,  $-(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_r\text{-C}_{3-10}$  carbocycle substituted with 0-2  $\text{R}^{\text{c}1}$ , or  $-(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_r\text{-5-10}$  membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $\text{S}(\text{O})_p$ , and substituted with 0-2  $\text{R}^{\text{c}1}$ ;

15  $r$ , at each occurrence, is selected from 0, 1, 2, and 3;  
 $s$ , at each occurrence, is selected from 0, 1, 2, and 3; and  
 $t$ , at each occurrence, is selected from 1, 2, and 3.

4. A compound according to Claim 3, wherein:

20  $\text{Q}$  is, independently at each occurrence, H, a  $\text{C}_{3-8}$  carbocycle substituted with 0-3  $\text{R}^{\text{d}}$ , or a 5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $\text{S}(\text{O})_p$ , and substituted with 0-3  $\text{R}^{\text{d}}$ ;

25  $\text{Q}^1$  is, independently at each occurrence, H, a  $\text{C}_{3-10}$  carbocycle substituted with 0-5  $\text{R}^{\text{d}}$ , or a 5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N,  $\text{NR}^{10}$ , O, and  $\text{S}(\text{O})_p$ , and substituted with 0-3  $\text{R}^{\text{d}}$ ;

30  $\text{Z}$  is phenyl substituted with 0-3  $\text{R}^{\text{b}}$ , naphthyl substituted with 0-5  $\text{R}^{\text{b}}$ , pyridyl substituted with 0-3  $\text{R}^{\text{b}}$ , thienyl substituted with 0-2  $\text{R}^{\text{b}}$ , thiazolyl substituted with 0-2  $\text{R}^{\text{b}}$ , oxazolyl substituted with 0-2  $\text{R}^{\text{b}}$ , isoxazolyl substituted with 0-2  $\text{R}^{\text{b}}$ , or imidazolyl substituted with 0-2  $\text{R}^{\text{b}}$ ;

$Z^a$  is phenyl substituted with 0-3  $R^c$ , naphthyl substituted with 0-3  $R^c$ , or a heterocycle substituted with 0-3  $R^c$  and selected from the group: furanyl, tetrahydrofuranyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, isoxazolyl, 4,5-dihydro-isoxazolyl, thienyl, triazolyl, thiadiazolyl, oxadiazolyl, pyridyl, pyrimidinyl, piperazinyl, piperidinyl, pyranyl, pyrazinyl, pyrazolyl, pyridoimidazolyl, pyrrolidinyl, pyrrolyl, indolyl, indolinyl, benzimidazolyl, benzothiazinyl, benzofuranyl, benzothiophenyl, benzoxazolyl, benzthiazolyl, benztriazolyl, benzisoxazolyl, benzisothiazolyl, quinolinyl, tetrahydroquinolinyl, isoquinolinyl, tetrahydro-isoquinolinyl, indazolyl, isobenzofuranyl, isoindazolyl, isoindolinyl, isoindolyl, methylenedioxyphenyl, quinazolinyl, 1,1-dioxido-2,3-dihydro-4H-1,4-benzothiazin-4-yl, 1,1-dioxido-3,4-dihydro-2H-1-benzothiopyran-4-yl, 3,4-dihydro-2H-chromen-4-yl, 2H-chromen-4-yl, and pyrazolo[1,5-a]pyridinyl;

$R^a$  is, independently at each occurrence, H,  $C_{1-6}$  alkyl, phenyl, or benzyl;

$R^{a1}$  is, independently at each occurrence, H,  $C_{1-6}$  alkyl, phenyl, or benzyl;

$R^{a3}$  is, independently at each occurrence, H,  $C_{1-6}$  alkyl, phenyl, or benzyl;

$R^c$  is, independently at each occurrence, H,  $OR^a$ , Cl, F, Br, =O,  $CF_3$ ,  $CH_2F$ ,  $CHF_2$ ,  $-(CR^aR^{a1})_rNR^aR^{a1}$ ,  $-(CR^aR^{a1})_rC(O)R^{a1}$ ,  $-(CR^aR^{a1})_rC(O)OR^{a1}$ ,  $-(CR^aR^{a1})_rC(O)NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rNR^aC(O)R^{a1}$ ,  $-(CR^aR^{a1})_rS(O)_pR^{a3}$ ,  $-(CR^aR^{a1})_rSO_2NR^aR^{a1}$ ,  $-(CR^aR^{a1})_rNR^aSO_2R^{a3}$ ,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl, phenyl substituted with 0-2  $R^{c1}$ , or a 5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$  and substituted with 0-2  $R^{c1}$ ;

alternatively, when two  $R^c$  groups are attached to the same carbon atom, they form a 5-6 membered carbocyclic or heterocyclic spiro ring C substituted with 0-2  $R^{c1}$  and consisting of carbon atoms, 0-4 ring heteroatoms selected from O, N, and  $S(O)_p$ , and 0-2 double bonds, provided that ring C contains other than a S-S, O-O, or S-O bond;

alternatively, when two  $R^c$  groups are attached to adjacent carbon atoms, together with the carbon atoms to which they are attached they form a 5-6 membered carbocyclic or heterocyclic ring D substituted with 0-2  $R^{c1}$  and consisting of carbon

atoms, 0-2 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, and 0-3 double bonds;

- $R^9$  is, independently at each occurrence, H,  $-(CR^aR^a)_rNR^aR^a$ ,  $-(CR^aR^a)_rC(O)(CR^aR^a)_sR^e$ ,  $-(CR^aR^a)_rC(O)OR^a$ ,  $-(CR^aR^a)_rC(O)NR^aR^a$ ,  $-(CR^aR^a)_rNR^aC(O)R^a$ ,  $-(CR^aR^a)_rS(O)_pR^a$ ,  $-(CR^aR^a)_rSO_2NR^aR^a$ ,  $-(CR^aR^a)_rNR^aSO_2R^a$ , C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl,  $-(CR^aR^a)_r$ -C<sub>3-7</sub> carbocycle substituted with 0-2 R<sup>c1</sup>, or  $-(CR^aR^a)_r$ -5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, and substituted with 0-2 R<sup>c1</sup>; and
- $R^{10}$  is, independently at each occurrence, H,  $-(CR^aR^a)_tNR^aR^a$ ,  $-(CR^aR^a)_tC(O)(CR^aR^a)_sR^e$ ,  $-(CR^aR^a)_tC(O)OR^a$ ,  $-(CR^aR^a)_tC(O)NR^aR^a$ ,  $-(CR^aR^a)_tNR^aC(O)R^a$ ,  $-(CR^aR^a)_tS(O)_pR^a$ ,  $-(CR^aR^a)_tSO_2NR^aR^a$ ,  $-(CR^aR^a)_tNR^aSO_2R^a$ , C<sub>1-6</sub> alkyl substituted with 0-2 R<sup>c1</sup>, C<sub>2-6</sub> alkenyl substituted with 0-2 R<sup>c1</sup>, C<sub>2-6</sub> alkynyl substituted with 0-2 R<sup>c1</sup>,  $-(CR^aR^a)_r$ -C<sub>3-10</sub> carbocycle substituted with 0-2 R<sup>c1</sup>, or  $-(CR^aR^a)_r$ -5-10 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, and substituted with 0-2 R<sup>c1</sup>.

5. A compound according to Claim 4, wherein:

- $R^2$  is Q<sup>1</sup>, C<sub>1-4</sub> alkylene-Q<sup>1</sup>, C<sub>2-4</sub> alkenylene-Q<sup>1</sup>, C<sub>2-4</sub> alkynylene-Q<sup>1</sup>,  $-(CH_2)_rO(CH_2)_s-Q^1$ ,  $-(CH_2)_rNR^a(CH_2)_s-Q^1$ ,  $-(CH_2)_rC(O)(CH_2)_s-Q^1$ ,  $-(CH_2)_rC(O)O(CH_2)_s-Q^1$ ,  $-(CH_2)_rC(O)NR^a(CH_2)_s-Q^1$ ,  $-(CH_2)_rNR^aC(O)(CH_2)_s-Q^1$ ,  $-(CH_2)_rS(O)_p(CH_2)_s-Q^1$ ,  $-(CH_2)_rSO_2NR^a(CH_2)_s-Q^1$ , or  $-(CH_2)_rNR^aSO_2(CH_2)_s-Q^1$ ;
- $R^3$  is H, C<sub>1-4</sub> alkyl, C<sub>2-4</sub> alkenyl, or C<sub>2-4</sub> alkynyl;
- $R^4$  is H or C<sub>1-4</sub> alkyl;
- $R^5$  is H or C<sub>1-4</sub> alkyl;

alternatively, R<sup>2</sup> and R<sup>3</sup>, together with the carbon atom to which they are attached, combine to form a 3-8 membered carbocyclic or heterocyclic ring consisting

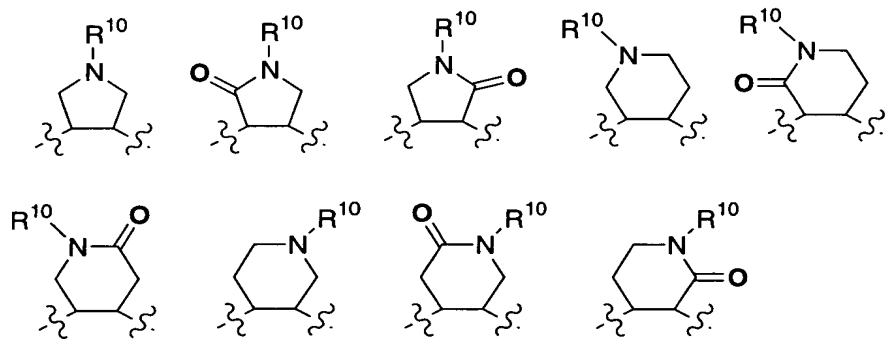


of carbon atoms, 0-2 ring heteroatoms selected from O, N, NR<sup>10</sup>, and S(O)<sub>p</sub>, and 0-2 double bonds;

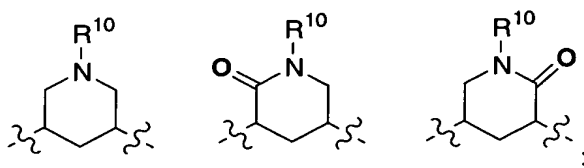
alternatively, R<sup>4</sup> and R<sup>5</sup>, together with the carbon atom to which they are attached, combine to form a 3-8 membered carbocyclic or heterocyclic ring consisting  
5 of carbon atoms, 0-2 ring heteroatoms selected from O, N, NR<sup>10</sup>, and S(O)<sub>p</sub>, and 0-2 double bonds;

Q<sup>1</sup> is, independently at each occurrence, H, a C<sub>3-6</sub> carbocycle substituted with 0-2 R<sup>d</sup>, or a 5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, NR<sup>10</sup>, O, and S(O)<sub>p</sub>, and  
10 substituted with 0-2 R<sup>d</sup>;

ring E is a C<sub>4-7</sub> cycloalkyl substituted with 0-2 R<sup>c</sup>, a C<sub>4-7</sub> cycloalkenyl substituted with 0-2 R<sup>c</sup>, phenyl substituted with 0-2 R<sup>c</sup>, or a heterocyclic ring substituted with 0-2 R<sup>c</sup> and selected from: furanyl, tetrahydrofuranyl, thienyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, isoxazolyl, pyrazolyl, pyrrolyl, pyridyl,  
15 pyranyl, tetrahydropyranyl, pyrimidinyl,



ring F a C<sub>4-7</sub> cycloalkyl substituted with 0-2 R<sup>c</sup>, a C<sub>4-7</sub> cycloalkenyl substituted with 0-2 R<sup>c</sup>, phenyl substituted with 0-2 R<sup>c</sup>, or a heterocyclic ring substituted with 0-2 R<sup>c</sup> and selected from: pyridyl, pyranyl, tetrahydropyranyl,  
20 pyrimidinyl,



- U is C(O), C(O)NR<sup>a1</sup>, NR<sup>a1</sup>C(O), S(O)<sub>p</sub>, S(O)<sub>p</sub>NR<sup>a1</sup>, or NR<sup>a1</sup>S(O)<sub>p</sub>;
- X is absent or is methylene;
- Y is absent or is O;
- Z is phenyl substituted with 0-3 R<sup>b</sup>;
- 5 U<sup>a</sup> is absent or is O;
- Y<sup>a</sup> is absent or is O;
- R<sup>a</sup> is, independently at each occurrence, H, or C<sub>1-4</sub> alkyl;
- R<sup>a1</sup> is, independently at each occurrence, H, or C<sub>1-4</sub> alkyl;
- R<sup>a3</sup> is, independently at each occurrence, H, C<sub>1-4</sub> alkyl, phenyl, or benzyl;
- 10 R<sup>c</sup> is, independently at each occurrence, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, OR<sup>a</sup>, Cl, F, Br, =O, CF<sub>3</sub>, CH<sub>2</sub>F, CHF<sub>2</sub>, NR<sup>a</sup>R<sup>a1</sup>, (CR<sup>a</sup>R<sup>a1</sup>)<sub>r</sub>C(O)R<sup>a1</sup>, (CR<sup>a</sup>R<sup>a1</sup>)<sub>r</sub>C(O)OR<sup>a1</sup>, (CR<sup>a</sup>R<sup>a1</sup>)<sub>r</sub>C(O)NR<sup>a</sup>R<sup>a1</sup>, (CR<sup>a</sup>R<sup>a1</sup>)<sub>r</sub>NR<sup>a</sup>C(O)R<sup>a1</sup>, (CR<sup>a</sup>R<sup>a1</sup>)<sub>r</sub>S(O)<sub>p</sub>R<sup>a3</sup>, (CR<sup>a</sup>R<sup>a1</sup>)<sub>r</sub>SO<sub>2</sub>NR<sup>a</sup>R<sup>a1</sup>, (CR<sup>a</sup>R<sup>a1</sup>)<sub>r</sub>NR<sup>a</sup>SO<sub>2</sub>R<sup>a3</sup>, or phenyl;
- alternatively, when two R<sup>c</sup> groups are attached to the same carbon atom, they
- 15 form a 5-6 membered carbocyclic or heterocyclic spiro ring C substituted with 0-2 R<sup>c1</sup> and consisting of carbon atoms, 0-4 ring heteroatoms selected from O, N, and S(O)<sub>p</sub>, and 0-2 double bonds, provided that ring C contains other than a S-S, O-O, or S-O bond;
- alternatively, when two R<sup>c</sup> groups are attached to adjacent carbon atoms,
- 20 together with the carbon atoms to which they are attached they form a 5-6 membered carbocyclic or heterocyclic ring D substituted with 0-1 R<sup>c1</sup> and consisting of carbon atoms, 0-2 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, and 0-3 double bonds;
- R<sup>e</sup> is, independently at each occurrence, H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, phenoxy,
- 25 benzoxy, C<sub>3-6</sub> carbocycle substituted with 0-2 R<sup>c1</sup>, or a 5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, and substituted with 0-2 R<sup>c1</sup>; and
- R<sup>10</sup> is, independently at each occurrence, H, -(CH<sub>2</sub>)<sub>t</sub>NR<sup>a</sup>R<sup>a1</sup>, -(CH<sub>2</sub>)<sub>r</sub>C(O)(CH<sub>2</sub>)<sub>s</sub>R<sup>e</sup>, -(CH<sub>2</sub>)<sub>r</sub>C(O)OR<sup>a1</sup>, -(CH<sub>2</sub>)<sub>r</sub>C(O)NR<sup>a</sup>R<sup>a1</sup>,
- 30 -(CH<sub>2</sub>)<sub>t</sub>NR<sup>a</sup>C(O)R<sup>a1</sup>, -(CH<sub>2</sub>)<sub>r</sub>S(O)<sub>p</sub>R<sup>a3</sup>, -(CH<sub>2</sub>)<sub>r</sub>SO<sub>2</sub>NR<sup>a</sup>R<sup>a1</sup>, -(CH<sub>2</sub>)<sub>t</sub>NR<sup>a</sup>SO<sub>2</sub>R<sup>a3</sup>,

C<sub>1-6</sub> alkyl substituted with 0-2 R<sup>c1</sup>, C<sub>2-6</sub> alkenyl substituted with 0-2 R<sup>c1</sup>,  
 C<sub>2-6</sub> alkynyl substituted with 0-2 R<sup>c1</sup>, -(CH<sub>2</sub>)<sub>r</sub>-C<sub>3-10</sub> carbocycle substituted with 0-2  
 R<sup>c1</sup>, or -(CH<sub>2</sub>)<sub>r</sub>-5-10 membered heterocycle consisting of carbon atoms and 1-4  
 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, and substituted  
 5 with 0-2 R<sup>c1</sup>.

6. A compound according to Claim 5, wherein:

R<sup>2</sup> is H, C<sub>1-4</sub> alkyl, C<sub>2-6</sub> alkenyl, or C<sub>2-6</sub> alkynyl;

R<sup>3</sup> is H or C<sub>1-4</sub> alkylene;

10 R<sup>4</sup> is H or C<sub>1-4</sub> alkyl;

R<sup>5</sup> is H or C<sub>1-4</sub> alkyl;

alternatively, R<sup>2</sup> and R<sup>3</sup>, together with the carbon atom to which they are  
 attached, combine to form a C<sub>3-7</sub> cycloalkyl, a C<sub>3-7</sub> cycloalkenyl, or a 5-6 membered  
 heterocyclic ring consisting of carbon atoms, 1 ring heteroatom selected from O, N,  
 15 NR<sup>10</sup>, and S(O)<sub>p</sub>, and 0-2 double bonds;

alternatively, R<sup>4</sup> and R<sup>5</sup>, together with the carbon atom to which they are  
 attached, combine to form a C<sub>3-7</sub> cycloalkyl, a C<sub>3-7</sub> cycloalkenyl, or a 5-6 membered  
 heterocyclic ring consisting of carbon atoms, 1 ring heteroatom selected from O, N,  
 NR<sup>10</sup>, and S(O)<sub>p</sub>, and 0-2 double bonds;

20 W is (CH<sub>2</sub>)<sub>m</sub>;

Y is absent;

Z is phenyl substituted with 0-1 R<sup>b</sup>;

Z<sup>a</sup> is phenyl substituted with 0-3 R<sup>c</sup>, naphthyl substituted with 0-3 R<sup>c</sup>, or  
 a heterocycle substituted with 0-3 R<sup>c</sup> and selected from the group: pyridyl, quinolinyl,  
 25 tetrahydroquinolinyl, isoquinolinyl, tetrahydro-isoquinolinyl, imidazolyl,  
 pyridoimidazolyl, benzimidazolyl, indolyl, indolinyl, 1,1-dioxido-2,3-dihydro-4*H*-  
 1,4-benzothiazin-4-yl, 1,1-dioxido-3,4-dihydro-2*H*-1-benzothiopyran-4-yl, 3,4-  
 dihydro-2*H*-chromen-4-yl, 2*H*-chromen-4-yl, pyrazolyl, and pyrazolo[1,5-*a*]pyridinyl;

R<sup>b</sup> is, independently at each occurrence, C<sub>1-6</sub> alkyl, OR<sup>a</sup>, Cl, F, Br, NR<sup>a</sup>R<sup>a1</sup>,  
 30 C(O)R<sup>a</sup>, C(O)OR<sup>a</sup>, C(O)NR<sup>a</sup>R<sup>a1</sup>, S(O)<sub>2</sub>NR<sup>a</sup>R<sup>a1</sup>, NR<sup>a</sup>S(O)<sub>2</sub>R<sup>a3</sup>, S(O)<sub>p</sub>R<sup>a3</sup>, or CF<sub>3</sub>;

$R^c$  is, independently at each occurrence,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $OR^a$ , Cl, F, Br, =O,  $CF_3$ ,  $-NR^aR^a1$ ,  $-(CR^aR^a1)_rC(O)R^a1$ ,  $-(CR^aR^a1)_rC(O)OR^a1$ ,  $-(CR^aR^a1)_rC(O)NR^aR^a1$ ,  $-(CR^aR^a1)_rNR^aC(O)R^a1$ ,  $-(CR^aR^a1)_rS(O)_pR^a3$ ,  $-(CR^aR^a1)_rSO_2NR^aR^a1$ , or  $-(CR^aR^a1)_rNR^aSO_2R^a3$ ;

5 alternatively, when two  $R^c$  groups are attached to the same carbon atom, they form a 5-6 membered carbocyclic or heterocyclic spiro ring C consisting of carbon atoms, 0-4 ring heteroatoms selected from O, N, and  $S(O)_p$ , and 0-2 double bonds, provided that ring C contains other than a S-S, O-O, or S-O bond;

alternatively, when two  $R^c$  groups are attached to adjacent carbon atoms, 10 together with the carbon atoms to which they are attached they form a 5-6 membered carbocyclic or heterocyclic ring D consisting of carbon atoms, 0-2 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ , and 0-3 double bonds;

$R^e$  is, independently at each occurrence, H,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy, phenoxy, benzoxy, phenyl substituted with 0-1  $R^{c1}$ , or a 5-6 membered heterocycle consisting 15 of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ , and substituted with 0-1  $R^{c1}$ ;

$R^{10}$  is, independently at each occurrence, H,  $-(CH_2)_rC(O)(CH_2)_sR^e$ ,  $-(CH_2)_rC(O)OR^a1$ ,  $-(CH_2)_rC(O)NR^aR^a1$ ,  $-(CH_2)_rS(O)_pR^a3$ ,  $-(CH_2)_rSO_2NR^aR^a1$ ,  $C_{1-4}$  alkyl substituted with 0-1  $R^{c1}$ ,  $C_{2-4}$  alkenyl substituted with 0-1  $R^{c1}$ ,  $C_{2-4}$  20 alkynyl substituted with 0-1  $R^{c1}$ ,  $-(CH_2)_r-C_{3-6}$  cycloalkyl substituted with 0-2  $R^{c1}$ ,  $-(CH_2)_r$ -phenyl substituted with 0-2  $R^{c1}$ , or  $-(CH_2)_r$ -5-6 membered heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ , and substituted with 0-2  $R^{c1}$ ;

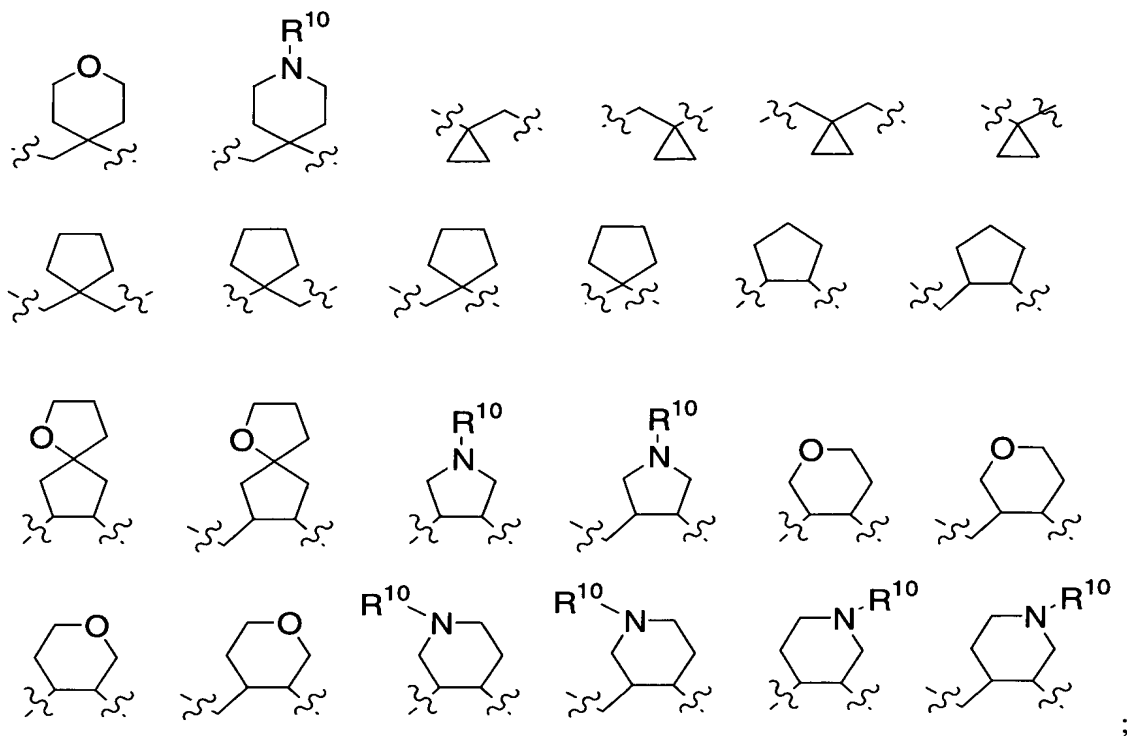
m, at each occurrence, is selected from 0, 1, and 2;

25 r, at each occurrence, is selected from 0, 1, and 2; and

s, at each occurrence, is selected from 0, 1, and 2.

7. A compound according to Claim 6, wherein:

L is selected from:  $-CH_2-$ ,  $-CH_2CH_2-$ ,  $-CH_2CH_2CH_2-$ ,  $-CH_2C(CH_3)_2-$ , 30  $-CH_2C(CH_3)_2CH_2-$ ,



W is (CH<sub>2</sub>)<sub>m</sub>;

Y is absent;

5 Z is phenyl substituted with 0-1 R<sup>b</sup>;

Z<sup>a</sup> is a heterocycle substituted with 0-3 R<sup>c</sup> and selected from the group:

quinolinyl, isoquinolinyl, and 1,1-dioxido-2,3-dihydro-4*H*-1,4-benzothiazin-4-yl; and

10 R<sup>10</sup> is H, methyl, ethyl, isopropyl, isobutyl, 2-propynyl, acetyl, 2,2-dimethylpropanoyl, t-butoxycarbonyl, 3-methylbutanoyl, isobutyryl, isonicotinoyl, phenoxyacetyl, methanesulfonyl, 3-pyridinylmethyl, 4-pyridinylmethyl, 3-pyridinylcarbonyl, 4-piperidinylcarbonyl, 4-morpholinylacetyl, 4-morpholinomethyl, or [1-(t-butoxycarbonyl)-4-piperidinyl]carbonyl.

15 8. A compound according to Claim 1, wherein the compound is selected from the group:

4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[3-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-propyl]-benzamide;

4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[2-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-ethyl]-benzamide;

- 4-(2-methyl-quinolin-4-ylmethoxy)-*N*-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-ylmethyl)-benzamide;
- N*-[1,1-dimethyl-2-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-ethyl]-4-(2-methyl-quinolin-4-ylmethoxy)-benzamide;
- 5 4-[4-(2-methyl-quinolin-4-ylmethoxy)-benzoylamino]-4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-ylmethyl)-piperidine-1-carboxylic acid *tert*-butyl ester;
- 4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-ylmethyl)-tetrahydro-pyran-4-yl]-benzamide;
- 4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[1-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-cyclopropylmethyl]-benzamide;
- 10 5-{1-[4-(2-methyl-quinolin-4-ylmethoxy)-benzenesulfonylmethyl]-cyclopentylmethyl}-2,4-dihydro-[1,2,4]triazole-3-thione;
- 4-[4-(2-isopropyl-benzoimidazol-1-ylmethyl)-benzoylamino]-4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-ylmethyl)-piperidine-1-carboxylic acid *tert*-butyl ester;
- 15 4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[*cis* 2-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-cyclopentyl]-benzamide;
- 4-(2-isopropyl-benzoimidazol-1-ylmethyl)-*N*-[2-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-cyclopentyl]-benzamide;
- 4-(2-methyl-quinolin-4-ylmethyl)-*N*-[2-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-cyclopentyl]-benzamide;
- 20 [1,2,4]triazol-3-yl)-cyclopentyl]-benzamide;
- 4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[2-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-cyclopentyl]-benzenesulfonamide;
- (3*S*,4*R*)-4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[3-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-tetrahydro-pyran-4-yl]-benzamide;
- 25 *trans*-4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[3-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-tetrahydro-pyran-4-yl]-benzamide;
- (5*R*,7*R*,8*S*)-4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[8-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-1-oxa-spiro[4.4]non-7-yl]-benzamide;
- 3 3-[4-(2-methyl-quinolin-4-ylmethoxy)-benzoylamino]-4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester;
- 30 4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-pyrrolidin-3-yl]-benzamide;

3-[4-(1,1-dioxo-2,3-dihydro-1*H*-1λ<sup>6</sup>-benzo[1,4]thiazin-4-ylmethyl)-benzoylamino]-4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester;

5 4-(1,1-dioxo-2,3-dihydro-1*H*-1λ<sup>6</sup>-benzo[1,4]thiazin-4-ylmethyl)-*N*-[4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-pyrrolidin-3-yl]-benzamide;

(3*S*,4*S*)-4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-pyrrolidin-3-yl]-benzamide;

(3*S*,4*S*)-*N*-[1-acetyl-4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-pyrrolidin-3-yl]-4-(2-methyl-quinolin-4-ylmethoxy)-benzamide;

10 (3*S*,4*S*)-4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[1-propyl-4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-pyrrolidin-3-yl]-benzamide;

*trans*-4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-pyrrolidin-3-yl]-benzamide;

15 (3*S*,4*S*)-3-[4-(2-methyl-quinolin-4-ylmethoxy)-benzoylamino]-4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-piperidine-1-carboxylic acid *tert*-butyl ester;

(3*S*,4*S*)-4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-piperidin-3-yl]-benzamide;

(3*S*,4*S*)-*N*-[1-acetyl-4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-piperidin-3-yl]-4-(2-methyl-quinolin-4-ylmethoxy)-benzamide;

20 (3*S*,4*S*)-4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[1-propyl-4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-piperidin-3-yl]-benzamide;

(3*S*,4*S*)-*N*-[1-methanesulfonyl-4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-piperidin-3-yl]-4-(2-methyl-quinolin-4-ylmethoxy)-benzamide;

25 (3*S*,4*S*)-*N*-[1-isopropyl-4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-piperidin-3-yl]-4-(2-methyl-quinolin-4-ylmethoxy)-benzamide;

(3*S*,4*S*)-4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[1-methyl-4-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-piperidin-3-yl]-benzamide;

(3*S*,4*R*)-4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[3-(5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-piperidin-4-yl]-benzamide;

30 4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[2-(5-oxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-cyclopentyl]-benzamide;

3-[4-(2-methyl-quinolin-4-ylmethoxy)-benzoylamino]-4-(5-oxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester; and  
 4-(2-methyl-quinolin-4-ylmethoxy)-*N*-[3-(5-oxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-tetrahydro-pyran-4-yl]-benzamide;

5

or a pharmaceutically acceptable salt form thereof.

9. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound according to Claim 1 or a  
 10 pharmaceutically acceptable salt form thereof.

10. A method for treating an inflammatory disorder, comprising: administering to a patient in need thereof a therapeutically effective amount of a compound according to Claim 1 or a pharmaceutically acceptable salt form thereof.

15

11. A method of treating a condition or disease mediated by MMPs, TACE, aggrecanase, or a combination thereof in a mammal, comprising: administering to the mammal in need of such treatment a therapeutically effective amount of a compound according to Claim 1 or a pharmaceutically acceptable salt form thereof.

20

12. A method comprising: administering a compound according to Claim 1 or a pharmaceutically acceptable salt form thereof, in an amount effective to treat a condition or disease mediated by MMPs, TACE, aggrecanase, or a combination thereof.

25

13. A method of treating according to Claim 12, wherein the disease or condition is selected from to as acute infection, acute phase response, age related macular degeneration, alcoholic liver disease, allergy, allergic asthma, anorexia, aneurism, aortic aneurism, asthma, atherosclerosis, atopic dermatitis, autoimmune disease,  
 30 autoimmune hepatitis, Bechet's disease, cachexia, calcium pyrophosphate dihydrate deposition disease, cardiovascular effects, chronic fatigue syndrome, chronic obstruction pulmonary disease, coagulation, congestive heart failure, corneal ulceration, Crohn's disease, enteropathic arthropathy, Felty's syndrome, fever,



fibromyalgia syndrome, fibrotic disease, gingivitis, glucocorticoid withdrawal syndrome, gout, graft versus host disease, hemorrhage, HIV infection, hyperoxic alveolar injury, infectious arthritis, inflammation, intermittent hydrarthrosis, Lyme disease, meningitis, multiple sclerosis, myasthenia gravis, mycobacterial infection, 5 neovascular glaucoma, osteoarthritis, pelvic inflammatory disease, periodontitis, polymyositis/dermatomyositis, post-ischaemic reperfusion injury, post-radiation asthenia, psoriasis, psoriatic arthritis, pulmonary emphysema, pyoderma gangrenosum, relapsing polychondritis, Reiter's syndrome, rheumatic fever, rheumatoid arthritis, sarcoidosis, scleroderma, sepsis syndrome, Still's disease, shock, 10 Sjogren's syndrome, skin inflammatory diseases, solid tumor growth and tumor invasion by secondary metastases, spondylitis, stroke, systemic lupus erythematosus, ulcerative colitis, uveitis, vasculitis, and Wegener's granulomatosis.

**14.** A method for treating inflammatory disorders, comprising: administering, to a 15 host in need of such treatment, a therapeutically effective amount of a compound of Claim 1 or a pharmaceutically acceptable salt form thereof, in combination with one or more additional anti-inflammatory agents selected from selective COX-2 inhibitors, interleukin-1 antagonists, dihydroorotate synthase inhibitors, p38 MAP kinase inhibitors, TNF- $\alpha$  inhibitors and TNF- $\alpha$  antibody or protein sequestration 20 agents.

**15.** An article of manufacture, comprising:

- (a) a first container;
- (b) a pharmaceutical composition located within the first container, wherein 25 the composition, comprises: a first therapeutic agent, comprising: a compound of Claim 1 or a pharmaceutically acceptable salt form thereof; and,
- (c) a package insert stating that the pharmaceutical composition can be used for the treatment of an inflammatory disorder.

30 **16.** An article of manufacture according to Claim 18, further comprising:

- (d) a second container;

wherein components (a) and (b) are located within the second container and component (c) is located within or outside of the second container.

17. An article of manufacture, comprising:
- 5 (a) a first container;
- (b) a pharmaceutical composition located within the first container, wherein the composition, comprises: a first therapeutic agent, comprising: a compound of Claim 1, or a pharmaceutically acceptable salt form thereof; and,
- (c) a package insert stating that the pharmaceutical composition can be used in
- 10 combination with a second therapeutic agent to treat an inflammatory disorder.
18. An article of manufacture according to Claim 20, further comprising:
- (d) a second container;
- wherein components (a) and (b) are located within the second container and
- 15 component (c) is located within or outside of the second container.